

## REMARKS

The Official Action and the exceptionally large number of formal rejections under '112 have been carefully reviewed. The review strongly indicates that the claims, as amended, recite patentable subject matter and should be allowed given the clear absence of prior art to the effect that, prior to the work of the present invention there has been no selection of and identified replacement of amino acid sites without non-native amino acids to result in increase catalytic activity. Reconsideration and allowance are therefore respectfully requested.

The invention pertains to a method that results in an increase in the specific activity of a mutated glycosyl hydrolase of an E1 endoglucanase on a cellulosic substrate relative to an unmutated form of the glycosyl hydrolase, by replacing an active site associated glycosyl-stabilizing amino acid of the glycosyl hydrolase with a replacing amino acid that binds cellobiose less tightly than the unmutated glycosyl-stabilizing amino acid.

The increased ability to solubilize cellulose, relative to their wild type counterparts, for instance, is for a number of glycohydrolases belonging to structural family 5 that have been identified as being structurally analogous to E1 and as having specific residues, the aromatic side chains of which may perform functions equivalent to that of Tyr-245 in E1 (Table 1 of specification). Mutation of these residues to the residues listed in rows of the middle column (Trp39 of 1A3H; Trp171 of 1BQC; Trp212 of 1CEN; Phe229 and/or Phe258 of 1CZ1; Trp259 and/or Trp811 of 1EDG; Trp30 of 2MAN) produce a decrease in the degree of product inhibition exhibited by the resulting mutant enzymes, relative to that

exhibited by the wild-type enzymes, and as a result exhibit improved performance in the hydrolysis of cellulose.

Claims 7 and 31 were rejected under the second paragraph of 35 USC 112 on allegations of indefiniteness; however, in view of the fact that claims 7 and 31 now recite the specific amino acid sequences, resulting from the glycosyl hydrolase mutant sites, the rejection is no longer applicable.

Claims 29 and 31 were rejected under the second paragraph of 35 USC §112 on allegations of indefiniteness; however, in view of the amendments made to these claims, it is now clear which specific amino acids were mutated.

Claims 3, 7, 29 and 31 were rejected under the first paragraph of 35 USC §112 on allegations that the specification is not enabling for a method of increasing the specific activity of the E1 endoglucanase; however, in view of the amendments made to these claims and the fact that the claims must be read with reference to the specification commencing at page 6, line 16 through page 7, line 16, together with the results in Tables 1-4 (which make abundantly clear, the method of increasing the specific activity of the E1 endoglucanase comprising the mentioned amino acid sequences), the rejection is no longer applicable.

Claims 3, 7, 29 and 31 were deemed so broad as to encompass compounds including glycosyl hydrolase from all sources; however, in view of the delimited amendments to these claims, the determination is no longer applicable.

Claim 3 was rejected under the first paragraph of 35 USC §112 on allegations of containing subject matter not described in the specification so as to convey that inventors had possession at the time of filing; however, in view of the fact that this claim now specifically recites activity of a specific glycosyl hydrolase, the rejection is no longer applicable.

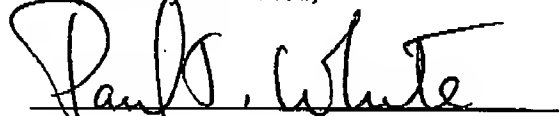
Note is taken of the request for a certified copy of the application under 35 USC 19(b). A certified copy has been ordered and will be submitted as soon as received from the USPTO.

Applicants further note the request for sequence compliance with the amino acids set forth in the claims, and such compliance has been made consistent with said request.

In view of the fact that no references have been cited in anticipation or obviousness of the invention – particularly as currently recited in the amended claims, it is believed that the application is now in condition for allowance, and early notification of the same is earnestly solicited.

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Respectfully submitted,



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